REMARKS

Applicants respectfully request reconsideration and allowance in view of this Amendment.

Applicants present their claims 94-121, 123, 124, and 129-136 for examination. Claims 104, 130 and 133 are amended.

Applicants appreciate the prior Examiner acknowledged the Supplemental Amendment was of record before the April 19, 2004 Final Rejection issued. The present Examiner has vacated the April 29, 2004 Final Rejection. Applicants appreciate this aspect of the May 24, 2006 PTO communication.

Previously amended claim 113 resolved the Section 112(2) rejection by amending the expression in question to delete the parenthesis so it *in hoc verba* reads "same cytokine superfamily," with it being understood that removing the parentheses had no limiting effect on the claim scope whereby no estoppel was created. Judging from the present Examiner's comments in the restriction requirement dated May 24, 2006, the former formality rejection (April 19, 2004 Office Action, pages 2, and 3-4) has been withdrawn. If not, then reconsideration is respectfully solicited.

Claim 104 recites gradually varying conditions. The recitation is consistent with what a person who is skilled in the art would know how to do based on the present specification. A person who is skilled in the art would be able to vary the reaction time, reagent concentrations, or pH during the course of the reaction, and do so gradually. Attention is courteously directed to the specification, including the gradually varying conditions recited in Example 1, Example 2 and Example 4. Reconsideration and withdrawal of the Section 112(2) and Section 112(1) rejections in the July 2, 2002 Off ice Action and the April 19, 2004 Office Action is courteously solicited.

Claims 107, 112-114 may recite "close proximity." Examples of 'close proximity' include, for instance, less than 10 Angstroms or less than 11 Angstroms, but it will be

appreciated that such literature-based examples are not intended as restricting the claim scope. The examples are offered to show that persons who are skilled in the art would understand the general metes and bounds of the claimed subject matter.

Previously amended claim 121 plus previously presented claim 135, and amended claim 130, overcome the Section 112(2) rejection in the July 2, 2002 Office Action and in the April 19, 2004 Office Action (pages 2 and 4). Reconsideration and withdrawal of the rejection are courteously solicited.

Applicants respectfully submit their application has already been previously scrutinized by Examiners, such as Examiners Budens and Brown, who have issued Office Actions. *See, e.g.*, Office Actions in 2001, 2002 and 2004, among others. Such Examiners considered the claims.

It is not seen that a requirement for restriction is either appropriate after other prior Examiners reviewed all the claims. Indeed, it is certainly not fair to impose a restriction requirement on a small entity well into patent prosecution, and well after other Office Actions on the merits, including a now withdrawn Final Rejection, and certainly it is inequitable to restrict claims after an Office Action on the merits for claims now under consideration.

Applicants have earlier suffered through the unavailability of their original, initial foreign patent agent (health reasons). Applicants have since tried to maintain their application alive while trying to obtain funding to move the technology towards commercial fruition. Under the circumstances, a restriction at this point in time years into prosecution is an unfortunate, unwanted financial burden on Applicants. It is respectfully submitted that the cost for separate prosecution and exposure to maintenance fees for multiple cases is, to put it delicately, a *de facto* tax.

Applicants have also considered the Katre document but find its citation odd in the context of an untimely requirement for restriction. In Applicants' view, the Katre reference does not furnish 'substantial evidence' to support the restriction requirement. *Arguendo*,

Katre at page 1, lines 3-5 refers to succinylation of IL-2 to render it soluble at physiological pH, but the methodology disclosed undermines the apparent thesis to the restriction requirement. For instance, at page 13, lines 27-28 Katre did not determine solubility of di-succinyl IL-2, and at page 8, lines 16-18 it's mentioned that cold storage at 4 °C for 3 days or physical agitation at RT causes visible precipitation of IL-2 protein, and does not appear to disclose or suggest gradually varying conditions (Applicants' claim 104, for example), inasmuch as Katre reports such ide variance in specific bioactivity (page 13, lines 15-18) as to call into question - in Applicants' present opinion, whether there was or was not even a measurable systematic difference between the materials being compared in Katre (page 13, lines 7-9). Put another way, inasmuch as the cited art apparently implies, if it does not suggest, deterioration of results by 30% of original activity, Applicants suggest the reference neither teaches the present inventions nor supports the restriction requirements, especially since it implies a modified substance clears faster from blood in testing. The Katre reference appears in Applicants' present opinion to be consistent with problems associated with the "SDS", which molecules are sometimes hard to remove thereby causing quantitative interpretations unreliable, as seen from the statement at page 12, lines 17-18 about trying to remove SDS. Accordingly, Applicants' present view is that a person skilled in the art would not have considered Katre as either a springboard to the present claimed inventions, or as a basis to slice this application into five (5) Groups years after other examiners have been able to examine the case and issued office actions on the merits.

Applicants furthermore courteously submit that even if an untimely restriction requirement were to be maintained, despite the prior scrutiny of the claims, that the Groups proposed should be reconsidered, re-formed, and consolidated in any event. For instance, the claims in Group I, Group IV and Group V are related. Group V is a subset of Group IV. Groups IV and V are exemplifications of what a person skilled in the art could obtain - following the teachings in the present specification - by practicing the Group I claimed inventions. Thus, these Groups of claims should be considered together.

Applicants therefore earnestly submit, *arguendo*, that at a minimum that Groups I, IV and V should be re-formed, and re-joined as one group. Accordingly, a methodology with electrospray mass spectroscopy (Group I), a protein hormone (Group IV) and a zinc binding

signal substance, *e.g.,* Zinc binding signal peptides (Group V), are proposed as the 'election,' on the basis of the reformed grouping of claims, assuming the restriction is not withdrawn in its entirety as it should be. (Contingently, and subject to traverse and to the request to reform the restriction requirement, electrospray mass spectroscopy, signal peptides and signal proteins, and zinc binding signal peptides are elected species.) Furthermore, on the assumption the claims are re-grouped, *arguendo* if the restriction is not withdrawn in its entirety - as it should be, at least claims 94-111, 112, 113, 114, 115, 116-117, and perhaps 118-120, 121, 123, perhaps 131, 133, perhaps 134 and 135, and 136.

Applicants courteously solicit reconsideration and withdrawal of the untimely requirement for restriction, and in the alternative reformation of the Groups so Groups I, IV and V are combined with the provisional elections as noted herein.

Respectfully submitted,

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